Journal of Arrhythmia 30 (2014) 82–87

Contents lists available at ScienceDirect

Journal of Arrhythmia

journal homepage: www.elsevier.com/locate/joa

Review

Identifying atrial arrhythmias versus pacing-induced rhythm disorders with state-of-the-art cardiac implanted devices

Ritsuko Kohno, MD, PhD[a,*], Yasushi Oginosawa, MD, PhD[b,1], Haruhiko Abe, MD, PhD[a,2]

[a] Department of Heart Rhythm Management, University of Occupational and Environmental Health, School of Medicine, 1-1, Iseigaoka, Yahatanishiku, Kitakyushu 807-8555, Japan

[b] The Second Department of Internal Medicine, University of Occupational and Environmental Health, School of Medicine, 1-1, Iseigaoka, Yahatanishiku, Kitakyushu 807-8555, Japan

ARTICLE INFO

Article history:
Received 6 January 2014
Accepted 10 February 2014
Available online 27 March 2014

Keywords:
Dual-chamber pacing
Atrial high rate episode
Repetitive non-reentrant ventriculo-atrial synchrony
Atrial tachyarrhythmia
Pacemaker mediated tachycardia

ABSTRACT

Repetitive non-reentrant ventriculo-atrial synchrony (RNRVAS) is a pacemaker-induced arrhythmia that must be distinguished from atrial fibrillation (AF). Pacemaker-induced arrhythmias are commonly detected as atrial high rate episodes (AHRE) by implanted cardiac devices. Two main types of atrial oversensing are recognized: far-field R-wave (FFRW) oversensing and pacemaker-induced arrhythmias, which include pacemaker-mediated tachycardia and RNRVAS. The presence of ventriculo-atrial conduction is required for both types of pacemaker-induced arrhythmias. The incidence of RNRVAS can increase with the use of various device settings and functions, such as long atrioventricular (AV) interval programming, the rate-adaptive mode, and the atrial overdrive pacing algorithm. The negative aspects of pacemaker-induced arrhythmias, especially RNRVAS, include (1) loss of optimal AV delay, (2) inappropriate increase in ventricular pacing, (3) induction of atrial arrhythmias, and (4) inaccurate diagnosis of AHRE. We review the incidence of arrhythmias, electrophysiological mechanisms, and the clinical diagnosis of RNRVAS identified by using dual-chamber implantable cardiac devices.

Contents

1. Introduction

The atrial high rate episode (AHRE) diagnostic function of implantable cardiac devices is often used to detect atrial tachyarrhythmias (ATA). However, its reliability and characteristics vary, depending on the device settings and use of other functions, such as the rate-adaptive mode or the atrial overdrive pacing (AOP) algorithm, especially in dual-chamber devices. The "*ASymptomatic atrial fibrillation and Stroke Evaluation in pacemaker patients and the atrial fibrillation Reduction atrial pacing Trial*" (ASSERT) examined the impact of device-detected, subclinical ATA on the development of strokes and systemic embolisms [1,2]. In that study, the presence of subclinical ATA was associated with a significant 2.5-fold higher risk of thromboembolic events in

* Corresponding author. Tel.: +81 93 691 7514; fax: +81 93 691 7547.
E-mail addresses: r-kohno@med.uoeh-u.ac.jp (R. Kohno), y-ogi@med.uoeh-u.ac.jp (Y. Oginosawa), haru-abe@med.uoeh-u.ac.jp (H. Abe).
[1] Tel.: +81 93 691 7436; fax: +81 93 691 6913.
[2] Tel.: +81 93 691 7514; fax: +81 93 691 7547.

http://dx.doi.org/10.1016/j.joa.2014.03.001
1880-4276

pacemaker or ICD recipients [2]. The diagnosis of subclinical ATA based on the presence of AHRE is critical information that should prompt the initiation of appropriate preventive therapies, such as long-term oral anticoagulation or antiarrhythmic medications.

The presence of AHRE, however, may not invariably indicate the presence of ATA. We have recently reported AHRE that reflected episodes of atrial fibrillation (AF) as well as device-mediated arrhythmic events, such as repetitive non-reentrant ventriculo-atrial synchrony (RNRVAS), pacemaker mediated tachycardia (PMT), and far-field R wave (FFRW) oversensing, particularly in the presence of long atrioventricular (AV) intervals in the DDD mode, or when rate-responsive pacing or an AOP algorithm was used in recipients of a dual-chamber pacemaker or an implantable cardioverter defibrillator [3]. RNRVAS or PMT require ventriculo-atrial (VA) conduction to develop.

2. Atrial setting in dual-chamber devices

An optimal setting of atrial sensitivity is key for the accurate detection of ATA by implantable dual-chamber pacing devices. To optimize AF detection and lower the risk of atrial undersensing by dual-chamber implanted devices, a setting of a <0.5 mV atrial sensitivity is usually recommended. The setting of a low atrial sensitivity lowers the risk of FFRW oversensing as well as lowering the chances of detecting ATA, due to undersensing the atrial electrogram during ongoing tachyarrhythmia. In this case, the incidence of ATA may be underestimated. Conversely, a setting of high atrial sensitivity increases the chances of detecting ATA and increases the likelihood of FFRW oversensing, in which case the incidence of clinical ATA may be overestimated. Although the optimal atrial sensitivity remains to be defined, a <0.5 mV setting is generally recommended for recipients of implantable devices who have a history of AF. However, high atrial sensitivity settings might cause atrial oversensing. Table 1 shows the pitfalls for diagnosing AF. In the presence of atrial undersensing (when the atrial sensitivity is low), the incidence of true AF cannot be detected accurately. Atrial oversensing may result in (1) double counts of the P wave, which includes RNRVAS and FFRW oversensing, or (2) sensing of myopotentials, lead noise, or electromagnetic interference. Atrial undersensing and oversensing may both interfere with the diagnosis of true AF.

Table 1
Atrial sensing in dual-chamber devices.

Atrial undersensing
• **True atrial fibrillation**
• **Functional atrial fibrillation**
Atrial oversensing
• **Repetitive non-reentrant VA synchrony (RNRVAS)**
• **Pacemaker mediated tachycardia (PMT)**
• **Far-field R wave (FFRW) oversensing**
• **Myotonic potentials**
• **Lead failure**
• **Electromagnetic interference**
• **Other**

3. Device-detected non-atrial fibrillation

State-of-the-art, implantable, dual-chamber cardiac devices provide useful diagnostic information, including the number and duration of automatic mode switch (AMS) episodes upon detecting ATA. However, to collect accurate diagnostic information, special attention must be paid to the device settings, to the presence versus absence of VA conduction, which when present, often represents RNRVAS or PMT, to the post-ventricular atrial blanking period (PVAB) and atrial sensitivity, and to the sensing of FFRW in the atrial channel. Preventing FFRW sensing by the atrial channel is challenging as it is inversely correlated with the duration of the PVAB and with the atrial sensitivity. Furthermore, the presence of VA conduction may cause RNRVAS or PMT. Although FFRW sensing, RNRVAS, and PMT are not ATA, they (a) are counted as ATA episodes by implantable monitoring devices, (b) might be the source of inaccurate diagnostic information and inappropriate AMS from DDD to DDI or VVI mode, and (c) may trigger ATA or cause pacemaker syndrome [4–14]. The clinical shortcomings associated with atrial oversensing are shown in Fig. 1.

Increasing the duration of PVAB might be an effective means of preventing FFRW oversensing in the atrial channel. However, this narrows the search window of atrial sensing, and shortens the window of ATA detection, which might decrease the likelihood of detecting ATA. Conversely, a short PVAB widens the search window of atrial sensing and of ATA detection, a setting that might decrease the specificity of ATA detection. In clinical practice, therefore, a $+25$ ms PVAB setting between the ventricular pacing spike and FFRW sensing is generally recommended [15].

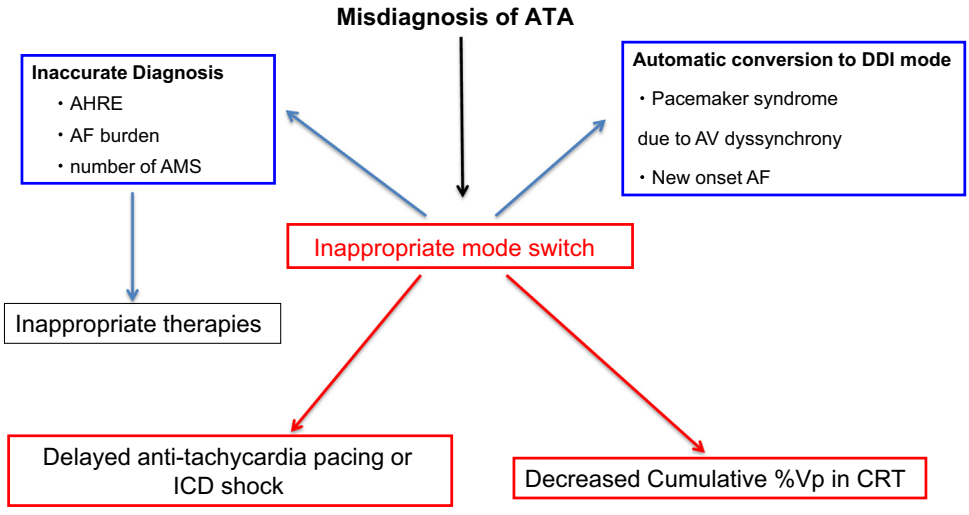

Fig. 1. Adverse effects of atrial oversensing. AHRE, atrial high rate episode; ICD, implantable cardioverter defibrillator; CRT, cardiac resynchronization therapy; AF, atrial fibrillation; AV, atrioventricular; AMS, auto mode switch; Vp, paced ventricular event.

Endless loop tachycardia, which might present as PMT or RNRVAS, both mediated by VA conduction, is a well known, understood, and relatively common complication associated with implantable dual-chamber cardiac devices. While PMT is the most commonly observed pacemaker-induced tachyarrhythmia, RNRVAS, also known as AV desynchronization arrhythmia or VA synchrony non-reentrant arrhythmia, may cause symptoms indistinguishable from those caused by PMT [16–18].

The occurrence of RNRVAS, first reported as an isolated case in 1985 [16], have since been confirmed in dual-chamber pacemaker recipients undergoing 24-h ambulatory electrocardiograms, who report symptoms similar to those of patients suffering from pacemaker syndrome [17,18].

4. Incidence of RNRVAS

RNRVAS is not an uncommon observation in dual-chamber pacemaker or ICD recipients [17,19]. We studied 39 patients who had neither histories nor occurrences of ATA before receiving dual-chamber pacemakers that were programmed in the DDD mode with AHRE set at >190 beats per minute (bpm) after implantation [14]. An atrial overdrive pacing (AOP) algorithm was randomly programmed "ON" in 19 and "OFF" in 20 patients. Of 1528 AHRE, 257 were available for analysis by using intracardiac electrograms (iEGM). Seventy-six episodes occurred with the AOP algorithm "OFF" and 181 occurred with the AOP algorithm "ON". Surprisingly, 109 of the 257 episodes (42%) were attributable to RNRVAS instead of AF episodes. In the AOP algorithm "OFF" group, 76 of 76 episodes (100%) were true ATA, whereas in the AOP algorithm "ON" group, 109 of 181 episodes (60%) were due to RNRVAS. The specificity of true ATA detection by using AHRE was 40% when the AOP algorithm was activated, versus 100% when it was not used, unequivocally confirming the significantly higher incidence of RNRVAS associated with the AOP activation.

Among 2343 pacemaker recipients followed up for a mean of 2.5 years in the ASSERT trial, 50% were randomly assigned to activation of the AOP algorithm, whereas in the other 50%, the algorithm was turned off [20]. The rate of false positive automatic detection of AF was 23.0% in the group assigned to the algorithm "ON", versus 7.7% in the group assigned to the algorithm "OFF" (relative risk 2.99; 95% CI 2.40–3.74; $P<0.001$). The cause of false positive automatic ATA detection was mainly due to 226 episodes of RNRVAS occurring in the AOP algorithm "ON" group, compared with 47 episodes in the AOP algorithm "OFF" group ($P=0.001$).

5. Electrophysiological mechanisms of RNRVAS

The electrophysiological mechanisms of RNRVAS have been thoroughly studied [17,21,22]. In dual-chamber pacing, it is usually observed in the presence of (1) VA conduction and retrograde P wave sensed within the post-ventricular atrial refractory period (PVARP), (2) additional programming in rate-adaptive mode or use of an AOP algorithm to prevent AF, and (3) programming of a long AV interval to prevent intrinsic AV conduction. The following additional conditions leading to the occurrence of RNRVAS are also notable: (1) setting of a long PVARP, (2) the presence of a long VA conduction time, (3) the presence of a long myocardial atrial refractory period, and (4) programming of a high lower pacing rate limit.

Fig. 2 illustrates a common trigger of RNRVAS by a premature ventricular complex (PVC) propagating through the AV node and arriving at the atrium within the PVARP. If the AOP algorithm has been activated, the premature event is recognized as a premature atrial complex within the PVARP, causing early atrial pacing by the algorithm. However, this early pacing attempt might fall in the atrial refractory period, particularly in the presence of prolonged atrial refractoriness, for instance in the case of treatment with antiarrhythmic drugs. Although this ineffective atrial pacing does not activate the atrium, ventricular pacing occurs in programmed AV intervals in DDD or DDI modes. This ventricular-paced event propagates through the AV node retrogradely and activates the atrium. These cyclic atrial and ventricular depolarizations will be repeated continuously. The pacemaker will count 2 atrial (the first from retrograde conduction by a PVC or by ventricular pacing and the second from ineffective atrial pacing) and 1 ventricular paced

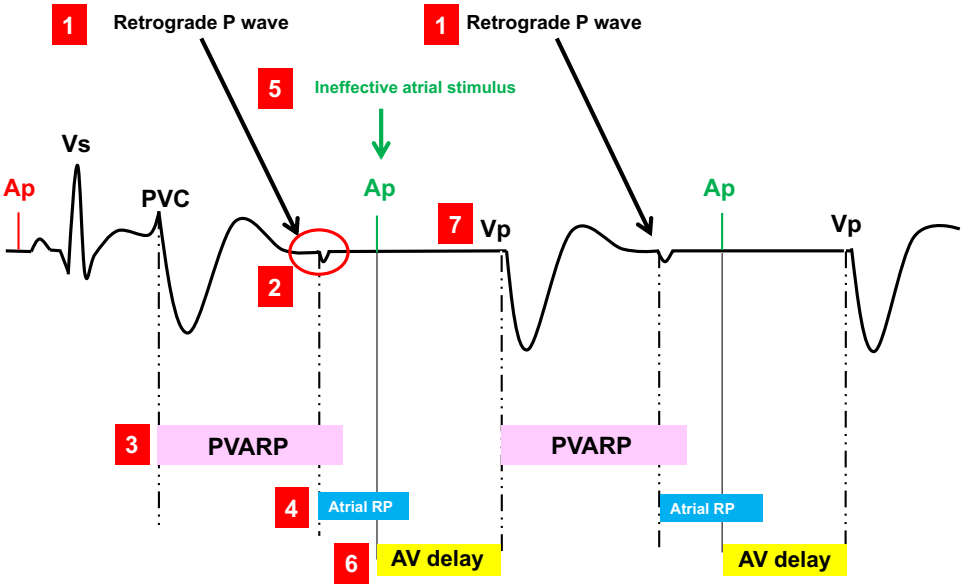

Fig. 2. Electrophysiological mechanism of repetitive non-reentrant ventriculo-atrial synchrony (RNRVAS). The retrograde P wave [1] from the PVC fell within the PVARP [2], which needs to be long enough [3]. After the atrial activation, the atrial refractoriness by the retrograde P wave persists [4]. The next early paced atrial event fell within the atrial refractory period, and that paced atrial event is ineffective [5]. After the ineffective atrial stimulus, a new timing cycle begins [6] and a paced ventricular event [7] occurs after the programmed atrioventricular interval. These cycles continue repetitively. Vp, paced ventricular event; Vs, sensed ventricular event; Ap, paced atrial event; As, sensed atrial event; PVARP, post-ventricular atrial refractory period; PVC, premature ventricular contraction; RP, refractory period.

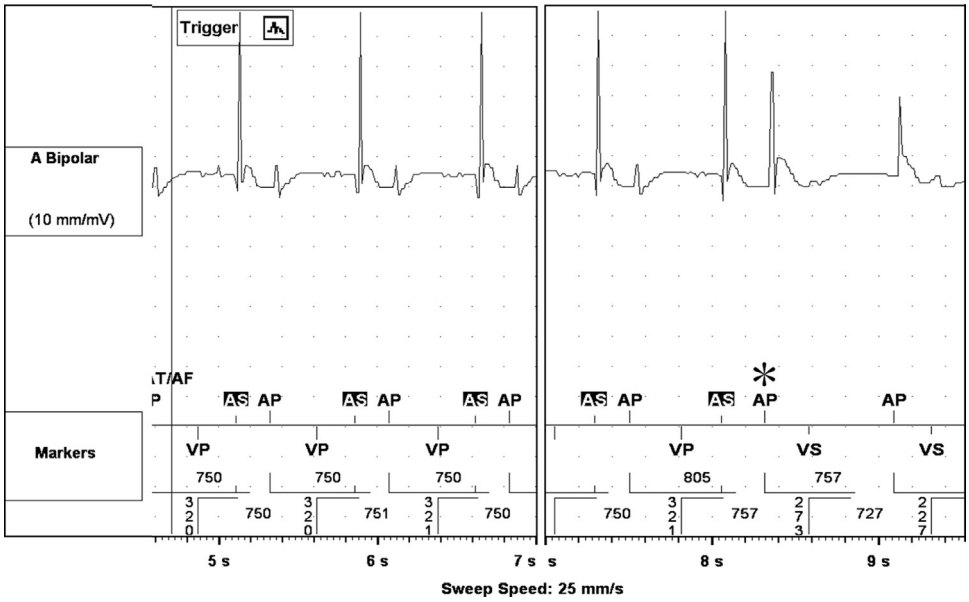

Fig. 3. Repetitive non-reentrant ventriculo-atrial synchrony (RNRVAS) induced by sensor-driven, rate-adaptive dual-chamber pacemaker. Top tracing: bipolar atrial electrogram channel (recorded between the tip and ring electrodes of the atrial lead). Bottom tracing: marker channel. VP, ventricular pacing; AS, atrial sensing (falling within the PVARP); AP, atrial pacing; ATA, device counts as ATA detection.

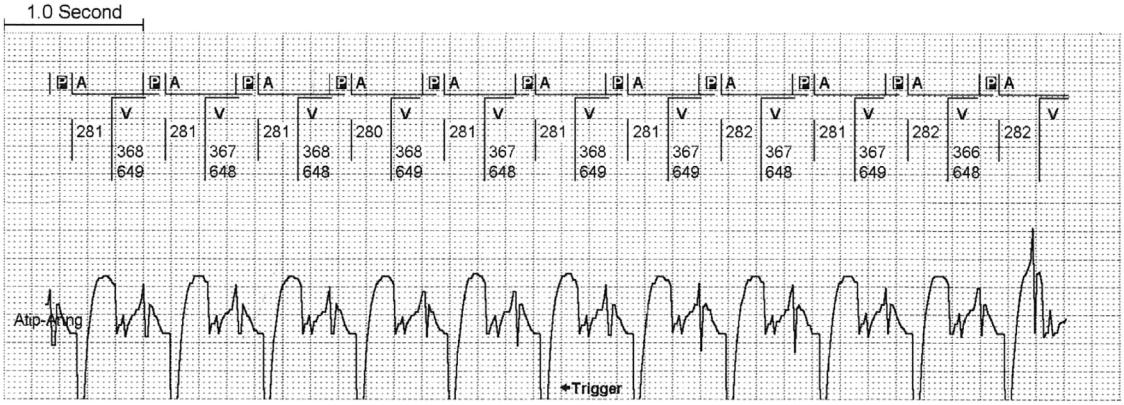

Fig. 4. Repetitive non-reentrant VA synchrony (RNRVAS) induced by atrial overdrive pacing algorithm. The retrograde P wave after ventricular pacing falls within the PVARP. Atrial overdrive pacing falls immediately after the sensed retrograde P wave. However, since the interval between that sensed P wave and the next paced atrial event is very short, the stimulus falls in the atrial myocardial refractory period and fails to capture the atrial myocardium. Ventricular pacing after an AV interval long enough for the atrial recovery allows the next retrograde VA conduction, resulting in sustained RNRVAS. Top tracing, marker chains; bottom tracing, intracardiac electrogram (iEGM). V, paced ventricular event; A, paced atrial event; P, sensed atrial event falling within PVARP; Atip-Aring, bipolar atrial recording between tip and ring of the atrial lead.

event. Thus, during RNRVAS, an atrial sensed and a non-captured atrial paced event occurs cyclically with ventricular paced event.

Fig. 3 shows an example of RNRVAS in a dual-chamber pacemaker recipient with sinus node disease, with the pacemaker set in rate adaptive DDI-R mode pacing with an AV interval of 300 ms and lower rate limit of 60 ppm. The tracing shows sensor-driven DDIR pacing at 80 bpm (V–V cycle length = 750 ms). Ventricular captures are conducted in a retrograde manner through the AV node, and the atrial events are sensed within the PVARP after a 220-ms VA conduction time. Rate adaptive atrial pacing is driven by a sensor at a rate of 80 ppm. Since the interval between the sensed retrograde P wave within the PVARP and the next atrial paced event is only 200 ms, the pacing stimulus does not capture the atrium. Ventricular pacing follows ineffective atrial pacing at the programmed AV delay of 320 ms. RNRVAS continues as long as the sensor-driven rate response is >80 ppm. However, after gradual slowing of sensor-driven pacing, the interval between the sensed P wave within the PVARP and the atrial paced event lengthens to >250 ms, allowing successful capture of the atrium (*), return to intrinsic AV conduction, and then terminate without VA conduction [23]. In this case, RNRVAS was induced with rate adaptive DDI-R pacing and observed in the setting of acceleration of sensor-driven DDD or DDDR dual-chamber pacing with long AV intervals [17,19].

Another example of RNRVAS, induced by the AOP algorithm set for the prevention of AF in DDD mode, is shown in Fig. 4 [3,14]. The retrograde P wave after ventricular pacing falls within the PVARP, activating the AOP algorithm. Since the interval between the sensed retrograde P wave and the next atrial paced event initiated by the AOP algorithm is very short, the atrial pacing stimulus falls in the atrial refractory period and fails to capture the atrium. Ventricular pacing after a programmed AV interval long enough for recovery of the atrial myocardium allows repetitive VA conduction and perpetuation of RNRVAS. While RNRVAS is not common, it is generally observed in the presence of VA conduction and retrograde P waves sensed within the PVARP, after ventricular pacing triggers the AOP algorithm, and when a relatively long AV interval has been programmed to limit

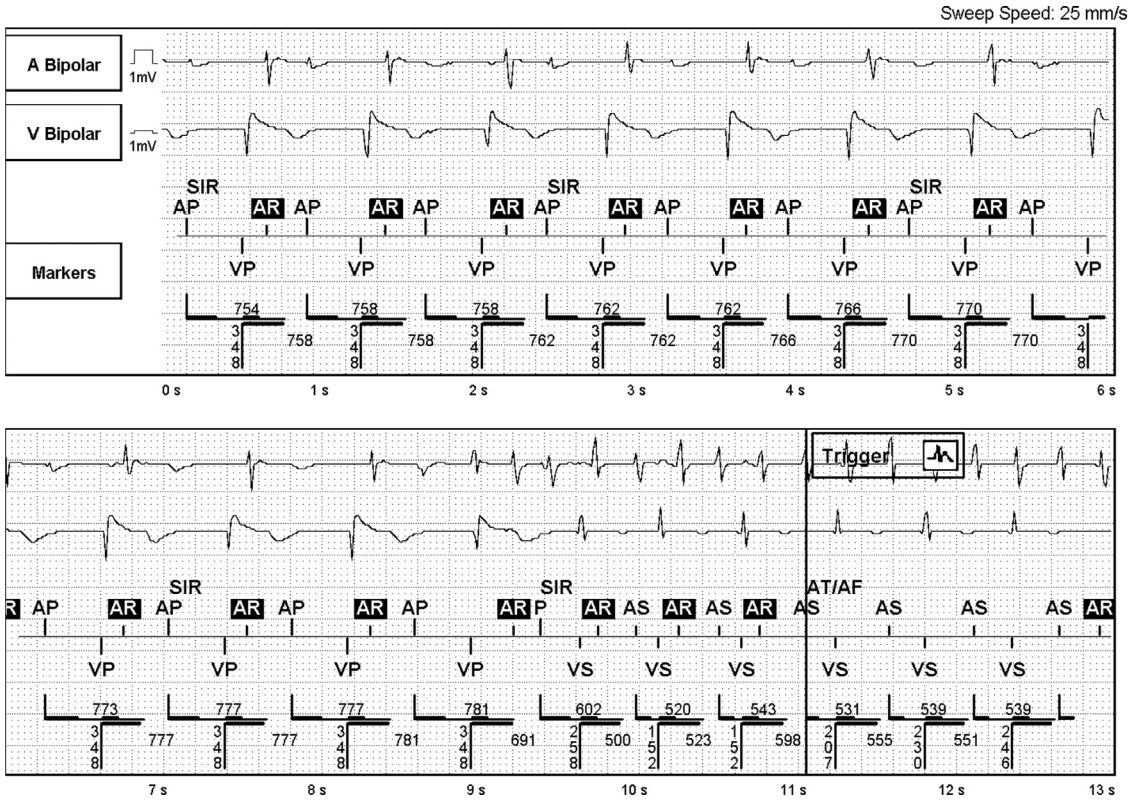

Fig. 5. Intracardiac electrogram recording of transition to atrial fibrillation from sustained repetitive non-reentrant VA synchrony (RNRVAS). In this case, the transition from sustained RNRVAS to AF was confirmed. This AT/AF event was sustained for 31 min 6 s. SIR, Sensor Indicated Rate; VP, ventricular pacing; VS, ventricular sensing; AR, atrial sensing (falling within the PVARP); AP, atrial pacing; AS, atrial sensing; AT/AF, device counts as AT/AF detection.

unnecessary ventricular pacing, particularly in instances of sinus node disease.

6. Clinical diagnosis of RNRVAS

RNRVAS is usually diagnosed by recording a 12-lead or a 24-h ambulatory electrocardiogram and is confirmed by interrogating the iEGM data stored in the pacemaker memory. It rarely causes symptoms, although it might emulate pacemaker syndrome. In most cases, RNRVAS is detected at the time of scheduled ambulatory visits.

Technologic advances in state-of-the-art pacemakers have facilitated the detection of RNRVAS, as the detection algorithm for AHRE is capable of counting both atrial sensed and paced events within the atrial refractory period.

7. Clinical implications

The potential adverse effects of RNRVAS are shown in Fig. 1 and include: (1) loss of optimal AV delay, (2) inappropriate increase in ventricular pacing, (3) trigger of atrial arrhythmias, (4) inaccurate diagnosis of AHRE, and (5) loss of optimal AV conduction by automatic switch from DDD to DDI or VVI modes. These adverse effects might increase unnecessary ventricular pacing and might affect ventricular function, especially in pacemaker recipients who present with sinus node disease and preserved AV conduction. The loss of optimal AV delay with RNRVAS causing pacemaker syndrome-like symptoms has been reported [24]. Furthermore, the repetitive occurrence of RNRVAS may cause AF (Fig. 5). In this case, the transition from sustained RNRVAS to AF was confirmed.

It is essential to distinguish between true AF and pacing-induced atrial arrhythmias when evaluating iEGMs of AHRE in clinical practice. Misdiagnosing AF in a case in which the true etiology is pacing-induced atrial arrhythmia, might lead to the use of anticoagulation therapies in pacemaker patients without true AF.

8. Summary

ATA are very common in recipients of implanted cardiac devices, and the detection of true AF, indicated by the presence of AHRE, is a useful diagnostic function of these devices. However, physicians should be aware that although AHRE can indicate true AF, the etiology can also be RNRVAS, PMT, and FFRW oversensing. Therefore, iEGM is a useful diagnostic tool available in advanced implanted cardiac devices.

Conflict of interest

All authors have no conflicts of interest to declare.

References

[1] Hohnloser SH, Capucci A, Fain E, et al. A Symptomatic atrial fibrillation and Stroke Evaluation in pacemaker patients and the atrial fibrillation Reduction atrial pacing Trial (ASSERT). Am Heart J 2006;152:442–7.
[2] Healey JS, Connolly SJ, Gold MR, et al. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med 2012;366:120–9.
[3] Kohno R, Abe H, Nagatomo T, et al. Repetitive non-reentrant VA synchrony and pacemaker-mediated tachycardia induced by the AF suppression algorithm. Pacing Clin Electrophysiol 2009;32:1333–5.
[4] Leung SK, Lau CP, Lam CT, et al. Programmed atrial sensitivity: a critical determinant in atrial fibrillation detection and optimal automatic mode switching. Pacing Clin Electrophysiol 1998;21:2214–9.
[5] Bordachar P, Cazeau S, Graindorge L, et al. Impact and prevention of far-field sensing in fallback mode switches. Pacing Clin Electrophysiol 2003;26:206–9.

[6] Kolb C, Aratma S, Zrenner B, et al. Prevention of far-field R wave sensing in the atrial channel of dual chamber pacemakers — an occasional cause of inappropriate mode switch. J Interv Card Electrophysiol 2004;10:231–5.
[7] Maury P, Schlaepfer J, Arbane M, et al. Incessant atrioventricular dissociation due to far-field QRS oversensing and recurrent mode switch in a dual chamber pacemaker. Europace 2002;4:149–53.
[8] Nash A, Fröhlig G, Taborsky M, et al. Rejection of atrial sensing artifacts by a pacing lead with short tip-to-ring spacing. Europace 2005;7:67–72.
[9] Brandt J, Worzewski W. Far-field QRS complex sensing: prevalence and timing with bipolar atrial leads. Pacing Clin Electrophysiol 2000;23:315–20.
[10] Cools FJ, Van Twembeke RR, Backers J, et al. Stability of far field R wave signals in different conditions. Europace 2003;5:175–83.
[11] Swerdlow CD, Schöls W, Dijkman B, et al. Detection of atrial fibrillation and flutter by a dual-chamber implantable cardioverter-defibrillator. For the Worldwide Jewel AF Investigators. Circulation 2000;101:878–85.
[12] Weretka S, Becker R, Hilbel T, et al. Far-field R wave oversensing in a dual chamber arrhythmia management device: predisposing factors and practical implications. Pacing Clin Electrophysiol 2001;24:1240–6.
[13] Ellenbogen KA, Mond HG, Wood MA, et al. Failure of automatic mode switching: recognition and management. Pacing Clin Electrophysiol 1997;20:268–75.
[14] Kohno R, Abe H, Oginosawa Y, et al. Reliability and characteristics of atrial tachyarrhythmias detection in dual chamber pacemakers. Circ J 2011;75:1090–7.
[15] Lau CP, Wang CC, Nqarmukos T, et al. A prospective randomized study to assess the efficacy of rate and site of atrial pacing on long-term development of atrial fibrillation. J Cardiovasc Electrophysiol 2009;20:1020–5.
[16] van Gelder LM, El Gamal MI. Ventriculoatrial conduction: a cause of atrial malpacing in AV universal pacemakers. A report of two cases. Pacing Clin Electrophysiol 1985;8:140–3.
[17] Barold SS. Repetitive reentrant and non-reentrant ventriculoatrial synchrony in dual-chamber pacing. Clin Cardiol 1991;14:754–63.
[18] Barold SS. Non-reentrant ventriculoatrial synchrony in dual chamber pacing. In: Santini M, Pistolese M, Alliegro A, editors. Progress in clinical pacing. Amsterdam: Excerpta Medica; 1990. p. 451–71.
[19] Barold SS, Levine PA. Pacemaker repetitive nonreentrant ventriculoatrial synchronous rhythm. A review. J Interv Card Electrophysiol 2001;5:45–58.
[20] Hohnloser SH, Healey JS, Gold MR, et al. Atrial overdrive pacing to prevent atrial fibrillation: insights from ASSERT. Heart Rhythm 2012;9:1667–73.
[21] Barold SS. Pacemaker induced repetitive nonreentrant ventriculoatrial synchrony: initiation and termination by ventricular extrasystole. Pacing Clin Electrophysiol 1997;20:989–92.
[22] Kohno R, Abe H, Oginosawa Y, et al. Failure of atrial capture during DDIR pacing in a patient with sinus node disease and preserved atrioventricular conduction. Pacing Clin Electrophysiol 2011;34:1301–3.
[23] Abe H. Detection of atrial tachyarrhythmias in an implantable monitoring device. J Arrhythmia 2012;28:19–25.
[24] Chien WW, Foster E, Phillips B, et al. Pacemaker syndrome in a patient with DDD pacemaker for long QT syndrome. Pacing Clin Electrophysiol 1991;14:1209–12.